

CLAIMS

1. Human spasmodic polypeptide (HSP) which has the amino acid sequence

Glu Lys Pro Ser Pro Cys Gln Cys Ser Arg Leu Ser Pro His Asn Arg
5 Thr Asn Cys Gly Phe Pro Gly Ile Thr Ser Asp Gln Cys Phe Asp Asn
Gly Cys Cys Phe Asp Ser Ser Val Thr Gly Val Pro Trp Cys Phe His
Pro Leu Pro Lys Gln Glu Ser Asp Gln Cys Val Met Glu Val Ser Asp
Arg Arg Asn Cys Gly Tyr Pro Gly Ile Ser Pro Glu Glu Cys Ala Ser
Arg Lys Cys Cys Phe Ser Asn Phe Ile Phe Glu Val Pro Trp Cys Phe
10 Phe Pro Asn Ser Val Glu Asp Cys His Tyr (SEQ ID NO:1)

or a functionally equivalent homologue thereof, characterized by being in glycosylated form.

2. HSP according to claim 1, characterized by being in N-glycosylated form.

15 3. HSP according to claim 1 or 2, which is glycosylated at Asn15.

4. HSP according to claim 3, in which the glycosylated side chain contains at least one hexose unit.

5. HSP according to claim 4, in which the glycosylated side
20 chain contains at least one mannose unit, preferably at least five mannose units, most preferably at least ten mannose units.

6. HSP according to claim 5, in which the glycosylated side chain contains 13-17 mannose units.

7. HSP according to claim 4, which in addition is glycosylated
25 with at least one unit of N-acetyl glucosamine (GlcNAc).

8. HSP according to claim 7, which is glycosylated with (GlcNAc)₂(Man)₁₀₋₁₅.
9. HSP according to claim 1, wherein Lys2 is replaced by Asn, Gln7 is replaced by Asn, Arg10 is replaced by Asn, Gly 20 is replaced by Thr or Ser, Gly23 is replaced by Asn, Ile 24 is replaced by Asn, Phe 36 is replaced by Asn, Asp 37 is replaced by Asn, Ser39 is replaced by Asn, Gln53 is replaced by Asn, Glu61 is replaced by Asn, Asp64 is replaced by Asn, Arg66 is replaced by Thr or Ser, Gly69 is replaced by Thr or Ser, Gly72 is replaced by Asn, Ile 89 is replaced by Thr or Ser, Pro98 is replaced by Asn or Val101 is replaced by Thr or Ser, or a combination of two or more of these substitutions.
10. HSP according to claim 9, wherein Asp64 is replaced by Asn, and wherein Arg66 is replaced by Thr or Ser.
11. HSP according to claim 9, in which the glycosylated Asn contains at least one hexose unit.
12. HSP according to claim 11, which is glycosylated with at least one mannose unit, preferably at least five mannose units, most preferably at least ten mannose units.
13. HSP according to claim 12, which is glycosylated with 13-17 mannose units.
14. HSP according to claim 11, which in addition is glycosylated with at least one unit of N-acetyl glucosamine (GlcNAc).
15. HSP according to claim 14, which is glycosylated with (GlcNAc)₂(Man)₁₀₋₁₅.
16. A variant of a spasmolytic polypeptide which is a fragment of human spasmolytic polypeptide (HSP) or porcine spasmolytic polypeptide (PSP) comprising at least one trefoil domain.

17. A variant according to claim 16, which comprises at least a sequence of amino acids from position 8 to 46 or from position 58 to 95.
18. A variant according to claim 16 or 17, wherein Asn15 is substituted by another amino acid, e.g. Asp or Glu.
19. A variant according to claim 16 or 17, wherein Thr17 is substituted by another amino acid except Ser, e.g. Ala.
20. A variant according to claim 16 or 17, wherein Arg10 is replaced by Asn, Gly 20 is replaced by Thr or Ser, Gly23 is replaced by Asn, Ile 24 is replaced by Asn, Phe 36 is replaced by Asn, Asp 37 is replaced by Asn, Ser39 is replaced by Asn, Glu61 is replaced by Asn, Asp64 is replaced by Asn, Arg66 is replaced by Thr or Ser, Gly69 is replaced by Thr or Ser, or Gly72 is replaced by Asn, or a combination of two or more of these substitutions.
21. A method of preparing a spasmolytic polypeptide in at least 60% glycosylated form, wherein a host cell transformed with a DNA fragment encoding a spasmolytic polypeptide and capable of providing glycosylation of said spasmolytic polypeptide is cultured under conditions permitting production of said spasmolytic polypeptide and recovering the resulting spasmolytic polypeptide from the culture.
22. A method according to claim 21, wherein the host cell is a fungal cell such as a yeast cell, e.g. a strain of Saccharomyces cerevisiae, or a filamentous fungus cell, e.g. a strain of Aspergillus, such as Aspergillus oryzae.
23. A pharmaceutical composition comprising HSP according to any of claims 1-15 together with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition comprising a variant spasmolytic polypeptide according to any of claims 16-20 together with a pharmaceutically acceptable carrier or excipient.

5 25. Use of HSP according to any of claims 1-15 for the manufacture of a medicament for the prophylaxis or treatment of gastrointestinal disorders.

26. Use of a variant spasmolytic polypeptide according to any of claims 16-20 for the manufacture of a medicament for the 10 prophylaxis or treatment of gastrointestinal disorders.

add A₂ >

ADD
C₂ >

ADD
C₅ >

add E₂ >